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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/720,411 | 03/12/2001 | Jan Tadeusz Czernuszka | 480821.90043 | 1013 |

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EXAMINER

KISHORE, GOLLAMUDI S

| ART UNIT | PAPER NUMBER |
|----------|--------------|
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1615

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DATE MAILED: 01/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/720,411

Applicant(s)

CZERNUSZKA ET AL.

Examiner

Gollamudi S Kishore, PhD

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 21 October 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1,2,6-12,14-16,18-23,25-30 and 34-38 is/are pending in the application.
- 4a) Of the above claim(s) 18-20 and 25 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 1,2,6-12,14-16,21-23,26-30 and 34-38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

The request for the extension of time dated 10-9-03, filing as an RCE dated 10-16-03 and the amendment dated 10-21-04 are acknowledged.

Claims included in the prosecution are 1-2, 6-12, 14-16, 21-23, 26-30 and 34-38. Claims 18-20 and 25 remain withdrawn.

Claim Rejections - 35 USC ' 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claims 1-2, 6-12, 14-16, 21-23, 26-29 and 34-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0 479 582 of record in combination with either of Eanes (Bone and Mineral, 17, pp., 269-272, 1992 of record) or Eanes (Calcif. Tissue Int (40, pp 43-48, 1987, also of record) in further combination with Chung (5,039,546).

EP discloses multilamellar liposomes containing an antibiotic. The liposomes are suspended in hydroxyapatite (hydroxy -calcium phosphate). The compositions are useful as dental implants (note the abstract, columns 4-7 and claims). What is lacking in

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EP is the teaching of the coating of the liposomes with apatite (calcium phosphate) instead of hydroxy-apatite. What are also lacking in EP are the teachings of the attachment of the liposomes to a surface.

As pointed out in the previous action, Eanes in both publications discloses liposomes coated with calcium phosphate; liposomes are made of phosphatidylcholine. The liposomes are suspended in NaCl and therefore, the surface layer containing chloride ions as recited in claim 6 is inherent in the prior art composition (note the abstract, and Table 1 on page 270 in Bone and Mineral; summary, Materials and Methods and discussion in Calcif. Tissue Int.). What is lacking in Eanes is the explicit teaching of the thickness of the coating of the vesicles by the calcium phosphate. However, on page 270, Eanes appear to suggest that the coating on the external surface is time dependent and PL dependent and therefore, it would have been obvious to one of ordinary skill in the art to obtain the vesicles with a desired coating thickness by varying the time and the selection of suitable phospholipids.

In essence, Eanes teaches the formation of coatings of calcium phosphate on the liposomal surface when suspended in calcium phosphate solutions.

Chung discloses that for dental implants (ceramic or metal) coated with either hydroxyapatite or calcium phosphate are known and routinely used in dental and orthopedic areas (note the abstract, columns 1-2 and claims).

The use of calcium phosphate instead of hydroxyapatite in EP would have been obvious to one of ordinary skill in the art since Eanes teaches that the liposomes can be coated with calcium phosphate and Chung teaches that both hydroxyapatite and

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calcium phosphates are routinely used in dental implant area. Further coating the composition of EP over a substrate would have been obvious to one of ordinary skill in the art, with a reasonable expectation of success since Chung teaches that either hydroxyapatite or apatite are coated on a substrate for use in dental and orthopedic areas. Chung does not disclose specifically the sizes of the implants. However, it is deemed to be within the skill of the art to use the desired sizes since sizes depend on the site the implant is to be used.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that the material in EP is entirely different from applicant's vesicles. Applicant points out to page 4, lines 26-28 and argues that it states "present invention is a system employing multi-lamellar liposomes having multiple encapsulating layers of aqueous dissolved antibiotic mixed in a suspension with hydroxyapatite and collagen and in contrast, applicant is concerned with individual vesicles which possess calcium phosphate as an outside layer formed on the inner layer of a phospholipid and which contain a pharmaceutically active compound within the vesicle. These arguments are not persuasive since the differences argued are not reflected in the claims. For instance, instant 'comprises' in claim 1 does not exclude multiple layers of phospholipid in the liposomes and the presence of collagen outside as taught in EP. Secondly, instant claim does not exclude the presence of calcium phosphate inside the vesicles and do not recite the thickness of the coating of calcium phosphate. Even assuming that the claim recites the thickness, the examiner points out that Eanes on page 270 appear to suggest that the coating on the external surface is time dependent and PL dependent

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and therefore, it would have been obvious to one of ordinary skill in the art to obtain the vesicles with a desired coating thickness by varying the time and the selection of suitable phospholipids.

Applicant argues that seeding of calcium phosphate, which penetrates the vesicle membrane, is not required in instant invention and that this difference is very significant one because the fact that calcium phosphate crystals work their way through the vesicle wall and Eanes makes it clear that the walls are ruptured. According to applicant, as a consequence of this is that, if one places pharmaceutically active material in vesicles, it would soon leak out. This argument is not found to be persuasive since applicant has not provided any experimental evidence to this effect. Furthermore, instant claims do not recite any specific amounts of the active agent encapsulated in the vesicles. The declaration submitted by Czernuszka is not found to be persuasive since the arguments in the declaration are not based on experimental evidence. Applicant provides no specific arguments with regard to Chung.

3. Claims 26-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0 479 582 of record in combination with either of Eanes (Bone and Mineral) or Calcif. Tissue Int., cited above and Chung (5,039,546), further in view of Redepenning (5,310,464).

The teachings of EP, Eanes and Chung have been discussed above. Chung in particular teaches the coating of calcium phosphate on metal or ceramic implants. What is lacking in the cited prior art is that the process of coating be conducted electrolytically.

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Redepenning discloses that when the metallic implants are coated by electrolytic process, the coating is superior to the coating obtained by conventional processes.

Redepenning's process involves immersing the implant in a solution of calcium and dihydrogen phosphate and coating the implant by electrolysis (note the abstract, col. 3, line 38 et seq; and claims).

The use of electrolysis for the coating of liposomes containing an outer layer of calcium phosphate over a metallic implant would have been obvious to one of ordinary skill in the art because Redepenning teaches that electrolytic process is superior to the conventional processes.


Applicant provides no specific arguments with regard to Redepenning. The rejection is maintained.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S Kishore, PhD whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 1234.


Gollamudi S Kishore, PhD
Primary Examiner
Art Unit 1615

GSK